**AUTISM AND ENVIRONMENTAL GENOMICS:**

**SYNERGISTIC SYSTEMS APPROACHES TO AUTISM COMPLEXITY**

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**This excerpt contains the abstract, keywords and points of interest only.**

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**ABSTRACT**

This chapter provides a framework for understanding how genomic and environmental factors may work together in autism spectrum disorders (ASD), via: 1) Gene-environment interactions (GxE) (genetic susceptibility to environment), 2) Environmental factors causing genetic damage in germ cells, 3) Environment causing heritable epigenetic modifications, and 4) Genetic traits influencing environmental exposure via behavior (“gene-environment correlation”). It is shown that high heritability does not exclude a high environmental contribution, and that common and preventable environmental exposures as well as genetic factors might both be etiologically essential. ASD research and progress toward prevention and intervention would benefit from greater collaboration, synthesis and prioritization of risk factors based on toxicology and population attributable fraction (PAF), along with a systems and pathway-based approach using bioinformatics and toxicogenomics, for which resources are included in this chapter.

**KEYWORDS**

1. Autism
2. Genetic susceptibility
3. Gene-environment interaction
4. Heritability
5. Environmental exposure
6. Environmental pollutants
7. Toxicology
8. Risk factor
9. Epigenetic
10. Bioinformatics

.**POINTS OF INTEREST**

1. Genomic and environmental factors work together in determining risk and severity of ASD. Four mechanisms are highlighted:
   1. Gene-environment interactions (GxE) (genetic susceptibility to environmental exposures)
   2. Environmental factors causing genetic damage in germ cells (including point mutations or structural changes)
   3. Environmental factors acting via heritable epigenetic modifications
   4. Genetic traits influencing environmental exposure via behavior (sometimes called “gene-environment correlation”).
2. The apparently high heritability of ASD is often misinterpreted as ruling out a large role for environmental risk factors. In fact, common, preventable environmental factors might be just as necessary as genetic factors for the occurrence of ASD, despite high heritability, because of gene-environment interplay:
   1. Heritability estimates mistakenly count gene-environment interaction as purely genetic for environmental exposures shared by twins.
   2. Many genetic contributors may actually depend upon environmental exposures to have an impact, making the exposures the root cause.
   3. Heritable epigenetic causes also may result from environmental exposures as the root cause.
   4. Shared placentas are an environmental factor that may boost MZ twin concordance and apparent heritability (through a different sort of gene-environment correlation). Genetic effects on a child’s individual (non-shared) social environment (traditional gene-environment correlations) also inflate apparent heritability.
3. Genetic findings in ASD should inform research on environmental pollutants (or other risk factors) and vice versa, since genes and pollutants may have common targets. Greater collaboration, synthesis, and prioritization of risk factors based on toxicology and population attributable fraction (PAF) would be valuable. A systems and pathway-based approach, using bioinformatics and toxicogenomics tools would also benefit ASD research.